PROJECT OCTAPHARMA: INTERVIEW WITH DOMINIQUE SIERAKOWSKI

“…the past is certain, but we only work for the future”

The project which has spanned several years is not yet complete. But nonetheless, it is clear that new process knowledge has been won which will find use in future projects with Octapharma. Because it is to an extent a “learning” project, Mr. Dominique Sierakowski gives an interim report in an interview, including background information and decision making parameters from his perspective as Head of Pharmaceutical Production.

Octapharma is a specialist for blood plasma products. The company is headquartered in Switzerland, and has in the last 30 years turned itself into a globally active research and production company with over 5,000 employees.

The project: A complete line with the capability of capping traditional aluminum caps and also the new Lyoseal plastic cap.

A 100 % IPC is used to monitor filling of the extremely expensive product. A stopper re-setting process minimizes rejects and maximizes product usage. The isolator area, which begins directly after the depyrogenation tunnel, encloses the 2-up peristaltic pump filling station as well as the closing station. The M+P isolator has an integrated H_2O_2 generator to decontaminate the machine surface and the interior of the isolator. With the use of the catalytic aeration process, considerably shorter H_2O_2 decontamination cycle times can be achieved. The capping unit processes both conventional stoppers and aluminum crimp caps but also Lyoseal plastic caps. Under laminar flow vials are transferred via a turntable to Klee freeze dryers. The same path is followed by conventionally stoppered vials. A coding machine and final tray loading complete the equipment. Processes are monitored by numerous optical inspections, while the environment is continuously monitored for the presence of airborne particles and viable organisms. The disposable product path with the peristaltic pumps outside of the isolator ensures that changeover time of product contact parts is max. 15 minutes. ▶

DOMINIQUE SIERAKOWSKI

Head of Corporate Pharmaceutical Production, Octapharma group

Biography

Dominique Sierakowski is Head of Corporate Pharmaceutical Production at Octapharma group. He is responsible for supporting production of parenteral liquid and freeze dried products in Octapharma plants and for implementation of new equipment in this area. He has been working in the manufacturing of parenteral products for over 35 years. During this time, he has developed knowledge and expertise in every field of aseptic processing such as sterilisation, aseptic filling, freeze drying and clean rooms.

Before joining Octapharma he held different positions in biopharmaceutical companies as head of production or project manager in industrial and improvement programs.

Questions to Octapharma, Mr. Sierakowski:

1. A project of mammoth proportions, but mainly a project which challenges common understanding of processes as they are implemented in the field today, and points to new directions – some of which may set new benchmarks. Can you describe some examples where new paths were taken instead of following the commonly treaded path?

First of all, we must remember all the time that all the decisions we make will impact the "business" for the next 15/20 years on a daily basis for quality, productivity, operating costs and working conditions for our personnel.

Some examples of new paths: Normally, isolators are highly recommended for long campaigns, a series of fills with the same product, same format, large batch size and long filling runs. We implemented isolator technology in the context of multi-products, multi-formats with high flexibility and strong productivity requirements. For sterile filtration and filling needles, a single use disposable system was chosen in order to increase flexibility.

A fully automatic loading and unloading system is commonly used for loading large freeze dryers. In our case, despite the fact that our freeze dryers are mid-sized to decrease aseptic risks during the loading as much as possible, a fully automatic loading and unloading system is implemented. After formatting of vials, a mobile cart transfers the vials from the filling machine via a loading corridor and loads the freeze dryer through a small door - "pizza door". After freeze-drying, a second mobile cart unloads and transfers vials via an unloading corridor to a de-formatting table before the capping process.

2. What was the motivation for deciding to try new concepts in aseptic filling technologies and freeze drying?

In 2004, the Food and Drug Administration announced a significant new initiative, CGMPs for the 21st Century, to enhance and modernize the regulation of pharmaceutical manufacturing and product quality with one of the objectives: encourage the early adoption of new technological advances by the pharmaceutical industry. Octapharma is investing in technologies that can objectively decrease contamination risk and optimize product savings. These were the goals when we decided on the use of new concepts in aseptic filling technologies and freeze drying.

3. Blood products are very specific pharmaceutical products. Which influence did the characteristics of the product have in the definition of the process? Were there specific goals for the product which you hoped to achieve with the new equipment?

Blood products are produced with human plasma; these products are from humans for humans. The mission of Octapharma is dedicated to developing life saving treatments, to enhance the quality of life for patients and also dedicated to the safe and optimal use of human proteins.

In addition, blood products are parenteral products produced through aseptic processing. We should never forget that aseptic processing is one of the most risky processes for the safety of the patients. As I said before, Octapharma is investing in technologies that can objectively decrease the risk of contamination and optimize product savings.

To reach these goals all decisions focus on "zero product loss" (as little loss of product as possible), accurate, simple and reliable machines which follow the "KISS design - Keep It Simple and Sterile". Machines had to be proven designs with robust technology: prototypes would not be taken into consideration.

4. You decided to use isolator technology, despite the fact that small as well as large batches of many different products are produced on the equipment. How do you achieve economic advantages?

We decided to implement isolator technology due to the proven sterility assurance level and better control of contamination risks, but also, because this is the current trend within aseptic processing and very probably the future expectations of auditors.

Economical operation could be achieved by reducing running cost on a daily basis: less floor space, less clean room area, less gowning, less monitoring.

Another important point for the economic impact is the comfort for personnel. By using isolators, people have better working conditions. As a result, we expect higher motivation and less staff turnover, an otherwise common situation due to demanding working conditions within aseptic areas. This avoids additional costs for training and qualification of new personnel.

5. Minimization of product loss, flexibility, and reduced decontamination or H_2O_2 cycle times for the isolator were surely essential to this project. Can you briefly outline the innovations

Correct, product loss and flexibility, linked to reduced decontamination or H_2O_2 cycle times, were essential for making all decisions. If we first consider the product loss, it was minimized due to the filling system accuracy and the special mode for starting and ending the filling. This included a filling system based on peristaltic pumps linked to load cells and a 100 % In Process Control system.

With respect to the flexibility and the reduced downtime between batches, several clever intricacies were implemented. There is no need to change format parts between different vial sizes within the isolator for vial sizes 6R to 100mL. Furthermore, conventional manual adjustment between sizes was replaced by automatic adjustment with servo motors. Two stopper stations are housed within the machine; each station runs a different size, so also in this case, there is no need to open the isolator to change parts. When parts have to be brought into the sealed isolator - for instance, materials for environmental monitoring processes, a material transfer lock with a fast H_2O_2 cycle provides maximum flexibility.

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Between batches, downtime is reduced by having the dosing system positioned outside of the isolator, and by using a disposable filling set. The short H_2O_2 cycle time of less than three hours also ensures that the machine can be ready for a new batch, quickly and securely.

Lastly, the minimization of the need for operator interventions underscores the flexibility and the operational time.

6. The pharmaceutical industry is very oriented towards process safety. Especially in freeze drying, redundant systems are commonly planned for. How can economical and process safety be guaranteed at the same time?

I will give you two examples. The installed freeze dryers are connected with a centralized cooling unit with a cascading principle, in which additional liquefied nitrogen, LN2, is used. This combination allows sudden peaks in cooling demand to be met by the LN2 module – without additional compressors. This design also allows the integration of redundancy for operational safety. In addition, the centralized cooling system is managed by a single control system. In comparison to several independent systems, the costs for software and validation of a single centralized cooling system are lower.

7. Taking the entire project into consideration, are there already some accomplishments, in whichever form, which you can call a true improvement, which you would also implement on future equipment?

Throughout these three years of design, construction and tests first at suppliers and now at site, a huge amount of successful teamwork has been achieved, including members from Octapharma and Optima. The current results demonstrate that we can achieve the expected results for filling accuracy and flexibility.

This project is however, far from its final objective. Current installations at two different sites need to be validated and submitted to authorities. Production is foreseen for the middle to end of 2014.

One other challenge in this project was to get harmonized equipment, process and documentation between the three supplier parts, filling line, isolator and freeze dryers, and also between the different Octapharma sites. This challenge has been clearly achieved. This successful harmonization fits the needs perfectly for growing and merged companies like Optima and Octapharma.

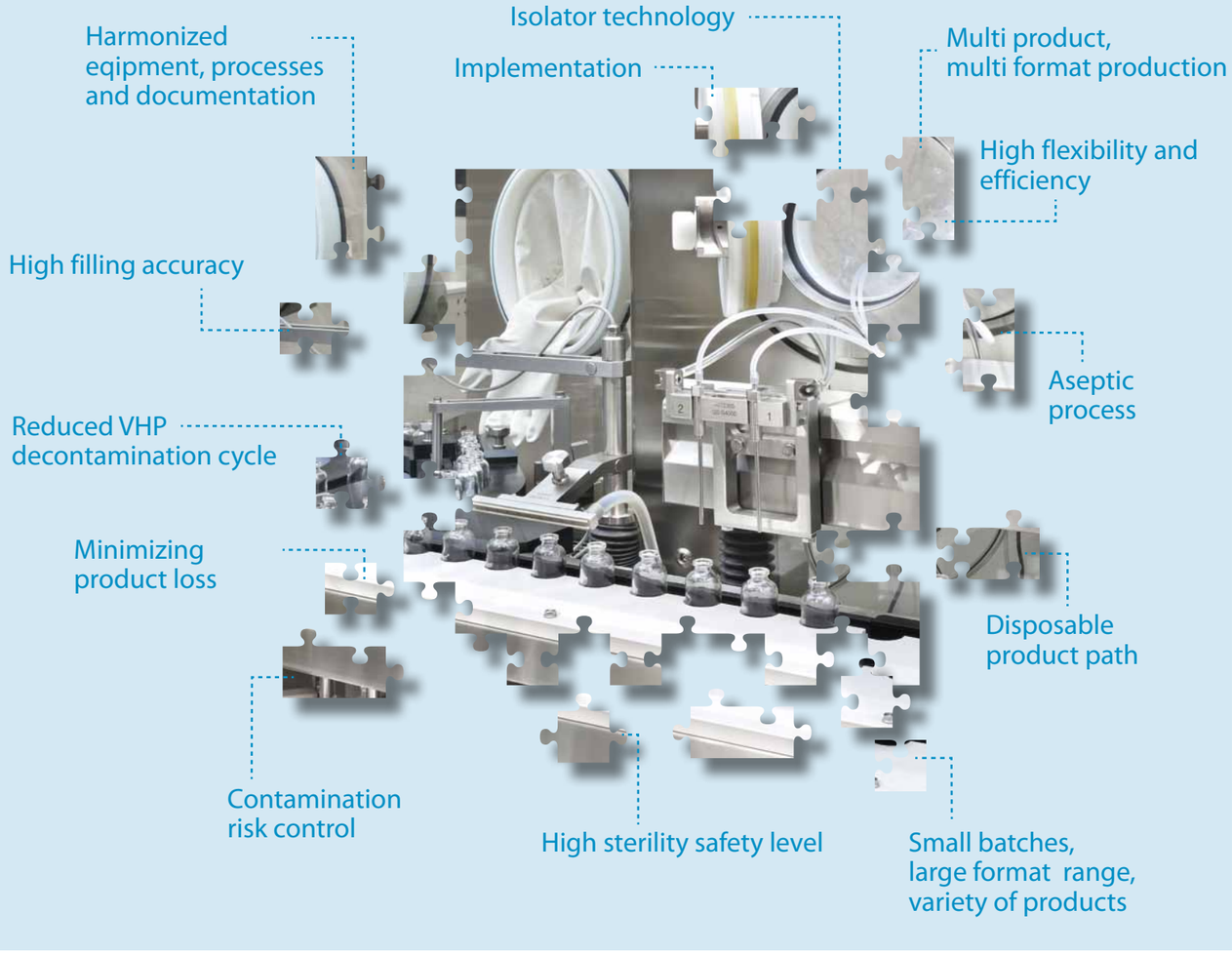
8. Which organizational rules / which approach do you consider essential for the success of such a project?

This is a global and strategic project for implementing new and harmonized filling-lines, barrier isolators and freeze-dryers at several Octapharma production plants. For the success of such a project, it is essential to develop a strong "partnership" between the customer and the supplier during the whole projects and the subsequent years. A "win-win" relationship is the obvious goal.

This goal was reached by implementing a mirrored organization between Octapharma and Optima: „One voice" from each party for all subjects ensured clear lines of communication. But organization is not enough. We needed to develop a strong team; the strength of the team comes from its multi-functional, multi-cultural role, and common, shared and clear objectives.

The project team set itself the following principles for teamwork, and has proven itself as the basis for a successful project:

- *Learning from the past and capitalizing on experiences*
- *Design and decisions based on science and finances*
- *Discussions and proposals based on hard facts and figures: no opinions*
- *We listen to one another, let the other person talk and help each other as far as possible.*
- *We work together as human beings; our teamwork is based on respect and trust.*



9. Was there any advice from Optima which was of particular value or importance to you?

It was much more the spirit of Optima, which is "process oriented" and fits to the needs of Octapharma, which we valued. The advanced technologies developed and implemented by Optima for manufacturing of high value products and the level of expertise of Optima people who listened attentively to customer expectations were of central importance.

10. Was an engineering consultancy involved in this project? Why did you decide for / against involving a consultancy?

We managed this project with Optima without an external consultant. At Octapharma, we think this project is the best opportunity to increase knowledge, to bring know-how and develop inter-personal skills. This is why we decided to create an internal Octapharma intersite team and try to manage this project by ourselves.

We also think that with a third party we would have increased the risk of misunderstandings. The current results confirm that this strategy is the right one and will be used as much as possible for following project steps. The team members involved have gained a great amount of satisfaction from the job.

Finally, it is a great experience both on a technical level and a human level.

11. In such an important project, selecting the right partner is an important success factor. What was your selection criteria?

To take advantage of the possibility for one supplier to cover the three main parts of our core equipment was a strong determiner, and as already mentioned the spirit of the Optima employees and orientation towards saving product.

The options proposed by the new technologies perfectly fit with our expectations, and were carried out by people with a high level of expertise. Last, but not least, the size and the structure of Optima is very similar to Octapharma; both are privately owned companies.

12. During your presentation at the Pharma Forum, you mentioned the (financial) risk of such a project. Would you, with your knowledge today where the project is not yet fully closed off, make the same decisions you did then? Is it already possible to draw conclusions?

That's a difficult question. This project is still far from its final objective, but I can say that now after almost four years' common work, we are still in a good partnership and we continue to progress and learn together. Let us speak again about this in 5 years! Because: The past is certain but we only work for the future.

Thank you very much, Mr. Sierakowski!